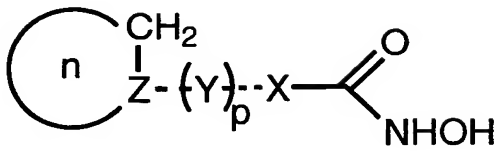
Claims

1. Compounds of the general formula (I)



or pharmaceutical acceptable salts or physiologically functional derivatives thereof wherein:

n is a non-aromatic ring system containing two to seven carbon atoms, wherein the ring system can contain one ore two double bonds;

X is C, CH or CH_2;

Y is selected from C, CH, CH_2, S, NR, CH_2-CH_2, H_2C--CH, HC--CH_2, C--CH_2, H_2C--C, or C--C; one or more of the hydrogen atoms can optionally be substituted by one or more substituents R`;

each of the dotted lines means a single, a double or triple bond with the exclusion of a combination of a triple with triple bond and a double with a triple bond;

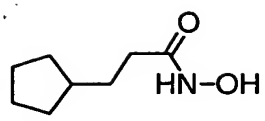
R` is independently H, -CN, alkyl, cycloalkyl, aminoalkyl, alkylamino, alkoxy, -OH, -SH, alkylthio, hydroxyalkyl, hydroxyalkylamino, halogene, haloalkyl, haloalkyloxy;

R is H, an alkyl or cycloalkyl group;

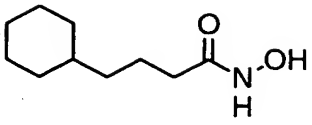
Z is CH, C, or P;

p is 0 or 1; and

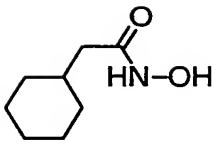
with the proviso that the following compounds are excluded:



and



and



2. The compound of claim 1, wherein n = cyclopentyl or cyclohexyl.

3. The compound of claim 1, wherein n = cyclopentyl or cyclohexyl and Z is CH.

4. A pharmaceutical composition comprising a compound as defined in any of claims 1 to 3 in free form or in the form of pharmaceutically acceptable salts or physiologically functional derivatives.

5. The use of a compound according to claim 1, including the compounds excluded in claim 1, as a medicament.

6. The use of a compound according to claim 1 as inhibitor of enzyms having histone deacetylase activity.

7. The use according to claim 5 in the treatment of a disease or a therapeutic indication in which inhibition of histone deacetylase activity is beneficial.

8. The use according to claim 5 wherein the human histone deacetylase is selected from the group consisting of HDACs 1-10 or a member of the SIR2 protein family.

9. The use of a compound according to claim 1 for the induction of differentiation of cells.

10. The use of a compound according to claim 1 as a medicament for the induction of differentiation of transformed cells.

11. The use of a compound according to claim 1 as a medicament for the induction of apoptosis of transformed cells.

12. The use of a compound according to claim 1 as a medicament for the inhibition of proliferation of transformed cells.

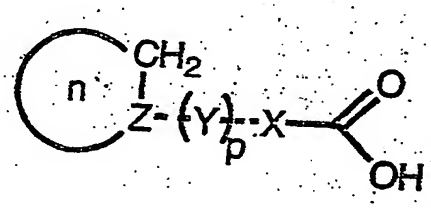
13. The use of a compound according to claim 1 for the inhibition of histone deacetylase activity.

14. The use of a compound according to claim 1 for the treatment of a disease or a therapeutic indication wherein the induction of hyperacetylation of histones has a beneficial effect.

15. The use of a compound according to claim 1 as a medicament for use in treatment of a disease or a therapeutic indication selected from the group consisting of skin cancer, melanoma, estrogen receptor-dependent and independent breast cancer, ovarian cancer, prostate cancer, renal cancer, colon and colorectal cancer, pancreatic cancer, head and neck cancer, small cell and non-small cell lung carcinoma, leukemias and other types of blood cell cancer and endocrine disease based on aberrant recruitment of histone deacetylase such as thyroid resistance syndrome.

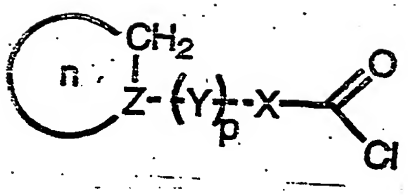
16. The use of a compound according to claim 1 for the inhibition of abnormal gene expression such as inflammatory disorders, diabetes, thalassemia, cirrhosis or protozoal infection.

17. A process for the preparation of a compound according to claim 1 which comprises the step of reacting an acid of formula (II)



formula (II)

(wherein n, X, Y, Z, and p are as defined in claim 1)
or an acid chloride of formula (III)



formula (III)

(wherein n, X, Y, Z, and p are as defined in claim 1)

with hydroxylamine.

18. A method for the treatment or prophylaxis of a condition where there is an advantage in inhibiting hyperacetylation of histones which comprises administering to a person an effective amount of a compound according to claim 1, including the compounds excluded in claim 1, or a physiologically acceptable salt or physiologically functional derivative thereof.